FLUORINE - CONTAINING HETEROCUMULENES COMMUNICATION 5.* A NEW SYNTHESIS OF BIS (TRIFLUOROMETHYL) KETENIMINES

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The bis (trifluoromethyl) ketenimines have proved to be interesting compounds which deserve a detailed study [1-3]. However, the few methods known for their preparation are fairly unsatisfactory and are based on the use of reactants that are not easily available [4-7].

In the present paper we studied the possibility of synthesizing the bis(trifluoromethyl)ketenimines by the reaction of perfluoroisobutylene with primary amines. The reaction of perfluoroisobutylene with aniline [8], ethylamine [9], hydroxylamine [10], and dimethylhydrazine [11] was studied previously. In all cases the perfluoroisobutylene was reacted with an excess of the amine, as a result of which the imidoyl fluorides of α -hydrohexafluoroisobutyric acid (II), or the products of their further reaction with excess amine, were usually obtained in low yields.

$$(CF_3)_2C = CF_2 + RNH_2 \rightarrow [(CF_3)_2CHCF_2NHR] \xrightarrow[-RNH_2]{RNH_3} (CF_3)_2CHCF = NR$$
(I)
(II)

We obtained entirely different results when this reaction was run with excess perfluoroisobutylene in the presence of catalytic amounts of triethylamine. Thus, the reaction of three moles of perfluoroisobutylene with a mole of aniline or p-anisidine in the presence of triethylamine, in ether solution, at room temperature, leads to the formation of either N-phenylbis(trifluoromethyl)ketenimine or its p-methoxy derivative, together with 2-hydroperfluoroisobutane.

$$3(CF_3)_2C = CF_2 + RNH_2 \xrightarrow{(C_2H_3)_3N} (CF_3)_2C = C = NR + 2(CF_3)_3CH$$
(III)

Under these conditions the imidoyl fluorides (II) undergo further dehydrofluorination by the triethylamine[†]; the triethylamine hydrofluoride formed hydrofluorinates the perfluoroisobutylene, with the regeneration of triethylamine.[‡] Although the reaction for the hydrofluorination of perfluoroisobutylene is reversible [13], the equilibrium in the system imidoyl fluoride (II) – perfluoroisobutylene – triethylamine is shifted toward the formation of the corresponding bis(trifluoromethyl)ketenimine (III), since 2-hydroperfluoroisobutane is a weaker CH acid than the imidoyl fluorides (II). As a result, a mixture of perfluoroisobutylene and a tertiary amine constitutes a specific reagent for the selective dehydrofluorination:

*See [1] for Communication 4.

† The dehydrohalogenation of imidoyl halides is one of the general methods for the synthesis of unfluorinated ketenimines [12].

‡ Evidently, the triethylamine plays a similar role in the dehydrofluorination of the initially formed adducts (I) to the imidoyl fluorides (II).

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Primary aliphatic amines react very vigorously with perfluoroisobutylene at low temperatures to give the corresponding imidoyl fluorides (II), but the formation of the N-alkylbis(trifluoromethyl)ketenimines in the presence of triethylamine is completed only by long heating at 100°. It is probable that in the sequence of steps that lead to the formation of the ketenimines (III) the determining step is that of proton cleavage from the imidoyl fluoride (II) by the tertiary amine, and consequently aryl substituents, which additionally stabilize the intermediate mesomeric anions (IV) due to conjugation, facilitate the dehydrofluorination reaction, whereas alkyl substituents, which do not take part in this stabilization, hinder the accomplishment of this reaction. In harmony with this,* the insertion of a methoxy group in the pposition of the aromatic ring of the N-arylimidoyl fluoride (II) retards the dehydrofluorination, while the insertion of a nitro group accelerates it. The size of the substituent attached to the nitrogen of the imidoyl fluoride (II) also plays a definite role. For example, in the presence of triethylamine, N-butylbis(trifluoromethyl)ketenimine is formed much more slowly than N-ethylbis(trifluoromethyl)ketenimine.

It should be mentioned that the use of pyridine as the catalyst, in place of triethylamine, leads in all of the cases studied only to the formation of the imidoyl fluorides (II); further dehydrofluorination fails to occur. As a result, by varying the ratio of the reactants, the character of the catalyst, and the reaction conditions, it is possible easily to obtain either the imidoyl fluorides (II) or the ketenimines (III) directly by the reaction of perfluoroisobutylene with primary amines.

The one-step synthesis convenient for the N-arylbis (trifluoromethyl) ketenimines is not always acceptable for the preparation of the N-alkylbis (trifluoromethyl) ketenimines. More drastic synthesis conditions cause the formation of secondary products and lower the yield of the ketenimines.[†] Consequently, their preparation by the dehydrofluorination of the imidoyl fluorides (II) with powdered KOH in ether at room temperature proved preferable on practical grounds. We note that neither by this method nor by the one-step method was it possible to obtain the pure N-p-nitrophenylbis (trifluoromethyl) ketenimine. This ketenimine, although it exists in ether solution on the basis of the data of the ¹⁹F NMR spectra, undergoes dimerization to the unsymmetrical dimer, the iminoazetidine (V), when its isolation is attempted. The symmetrical dimer, namely diazetidine (VI), is obtained by treating an ether solution of the ketenimine with pyridine (cf. [2]). It is interesting to mention that the symmetrical dimer (VI) rearranges to the unsymmetrical dimer (V) in the presence of hexametapol at room temperature



A similar isomerization for the symmetrical dimers of the N-phenyl- and N-p-methoxyphenylbis-(trifluoromethyl)ketenimines could not be accomplished even on long heating.

EXPERIMENTAL METHOD

The IR spectra were taken on a UR-20 instrument. The ¹⁹F NMR spectra were recorded on a Hitachi H-60 instrument that operated at a frequency of 56.46 MHz. The chemical shifts are given in parts per million from CF₃COOH (external standard). The GLC analysis was run on an LKhM-8M chromatograph using a column packed with Fluorosilicone deposited on Aeropak; He served as the carrier gas.

^{*} N-Phenylhydrazidoyl fluoride is not dehydrofluorinated by perfluoroisobutylene in the presence of triethylamine when heated at 100° (10 h).

[†] The bis(trifluoromethyl)ketenimines are dimerized when treated with tertiary amines [2]. Cycloaddition to them of perfluoroisobutylene, which is catalyzed by triethylamine, is another possible side reaction.

Imidoyl Fluorides of α -Hydrohexafluoroisobutyric Acid (II). To 0.11 mole of perfluoroisobutylene in 40 ml of absolute ether, containing several drops of pyridine, a solution of 0.05 mole of the amine in 20 ml of absolute ether was added, with stirring and cooling, at a rate such that the temperature of the reaction mixture did not exceed -10 to 0°. The mixture was stirred at this temperature for 1 h and then kept at ~20° for 2-3 h. The volatile products and the ether were distilled through a column, and the residue was distilled. The properties of the obtained imidoyl fluorides (II) are given in Table 1.

Dehydrofluorination of Imidoyl Fluorides (II) with Potassium Hydroxide. With vigorous stirring and cooling in iced water, 0.25 mole of powdered KOH was added gradually to a solution of 0.05 mole of the imidoyl fluoride (II) in 40-50 ml of absolute ether. The reaction mass was stirred for ~ 1 h at $\sim 20^{\circ}$ (the completeness of reaction was checked by GLC), after which the precipitate was filtered and washed with ether, and the filtrate was distilled. The properties of the compounds obtained are given in Table 2.

<u>Preparation of Bis(trifluoromethyl)ketenimines by Reaction of Perfluoroisobutylene with Primary</u> <u>Amines</u>. a) With stirring, a solution of 2.3 g of methylamine in 25 ml of absolute ether was added in drops to 45 g of perfluoroisobutylene and 0.1-0.2 ml of triethylamine in 50 ml of absolute ether, maintaining the temperature of the reaction mixture at -60 to -50° . The temperature of the mixture was brought up to $\sim 20^{\circ}$ and then it was heated in a glass ampul for 7-8 h on the steam bath. Distillation gave 3.9 g (29%) of N-methylbis(trifluoromethyl)ketenimine with bp 96-98°; 54-57° (165 mm); n_{25}^{25} 1.3344 [6].

N-Ethylbis(trifluoromethyl)ketenimine was obtained in a similar manner, in 54% yield.

b) With cooling in ice water, 1.5 g of aniline was added to a solution of 10 g of perfluoroisobutylene and several drops of triethylamine in 20 ml of absolute ether. According to the GLC data, after 40 min the solution contained a mixture of 76% of N-phenylbis(trifluoromethyl)ketenimine and 24% of the imidoyl fluoride (II), while after 150 min the amounts were respectively 97% and 3%. Subsequent distillation gave 3.6 g (90%) of N-phenylbis(trifluoromethyl)ketenimine with bp $50-52^{\circ}$ (5 mm).

In a similar experiment with p-anisidine the amount of N-p-methoxyphenylbis(trifluoromethyl)ketenimine in the mixture with the corresponding imidoyl fluoride was 37% after 40 min, 82% after 150 min, and 95% after 300 min. Subsequent distillation gave 89% of N-p-methoxyphenylbis(trifluoromethyl)ketenimine.

 $\underbrace{2,4-\text{Bis}(\text{hexafluoroisopropylidene})-1,3-\text{bis-}(\text{p-nitrophenyl})-1,3-\text{diazetidine}(VI)}_{1,3-\text{diazetidine}(VI)}. With cooling in ice, 2.6 g of perfluoroisobutylene and 10 drops of triethylamine were added to a solution of 3.2 g of the p-nitro-imidoyl fluoride (II) in 15 ml of absolute ether. The ¹⁹F NMR spectrum of the reaction mixture after 2 h was: -21.5 ppm (singlet) of N-p-nitrophenylbis(trifluoromethyl)ketenimine. Pyridine (1 ml) was added to the mixture and the next day the precipitate was filtered. We obtained 2.4 g (80%) of diazetidine (VI) with mp 268-271° (from acetone). Infrared spectrum (<math>\nu$, cm⁻¹): 1540 (NO₂), 1645 (C=C). ¹⁹F NMR spectrum (in hexametapol): -24.8 (singlet). Found: C 39.86; H 1.23; F 38.43; N 9.38%. C₂₀H₈F₁₂ · C₂₀H₈F₁₂ · N₄O₄. Calculated: C 40.27; H 1.34; F 38.25; N 9.4%.

 $\frac{1-p-\text{Nitrophenyl-2-hexafluoroisopropylidene-3,3-bis(trifluoromethyl)-4-p-nitrophenyliminoazetidine}{(V)}.$ a) A solution of 3.2 g of the p-nitroimidoyl fluoride (II) in 10 ml of ether was gradually added to a suspension of 4 g of powdered KOH in 15 ml of absolute ether. After 2 h the precipitate was filtered and washed with ether. From the filtrate 1.59 g (51%) of azetidine (V), mp 165-167° (from alcohol), was isolated. Infrared spectrum (ν , cm⁻¹): 1590 (NO₂), 1665 (C = C), 1780 (C = N). ¹⁹F NMR spectrum (in dioxane): -13.7 ppm [(CF₃)₂C, quartet]; -19.4 ppm (CF₃C=, multiplet); -23.6 ppm (CF₃C=, quartet). Found: C 40.19; H 1.47; F 38.56%. C₂₀H₈F₁₂N₄O₄. Calculated: C 40.26; H 1.34; F 38.25%.

b) Diazetidine (VI) (0.1 g) was dissolved in 1 ml of hexametapol. Based on the ¹⁹F NMR data, after 2 h the solution still contained about a third of the diazetidine (VI); after a day the rearrangement was complete.^{*} The solution was poured into water and the obtained crystals were filtered. We obtained 0.06 g (60%) of azetidine (V), mp 164-166° (from alcohol), which was identical with the compound obtained in the preceding experiment.

Dehydrofluorination of Imidoyl Fluorides (II) with Pyridine. a) To 1.4 g of the N-p-nitrophenylimidoyl fluoride (II), 1 ml of pyridine was added. After 2 days the precipitate obtained was filtered. We obtained 0.9 g (69%) of crystals with mp 165-166° (from alcohol), which were identical with the above obtained azetidine (V).

* The symmetrical dimers of the N-phenyl- and N-p-methoxyphenylbis (trifluoromethyl) ketenimines do not change when heated with hexametapol at 100° (8 h).

T	Tield,	Bp, °C	IR spectrum,	¹⁹ F NMR s (in CCl ₄),	pectrum ô, ppm		Foun	d, %		Empirical	υ	alculat	ed,%	
억	d'o	(p, mm Hg)	$\nu_{\rm cm}$	CF.*	CF †	υ	Ħ	<u>Б</u>	N	formula	σ	н	÷.	z
CH_{3} $\operatorname{Ce}_{2}\operatorname{H}_{3}$ [9]	$ \begin{bmatrix} 43, 5 \\ 38, 6 \end{bmatrix} $	63-65 77-80	1750	-11,2	47 49,3	·						-		
C4H, C6H11	20	61-63 (95) 82-87 (50)	1730	-12,0 -13,1	48,5 48,5	42,95	4,05	I	5,06	$\mathrm{C}_{10}\mathrm{H_{12}F_7N}$	43,1	4,31	. 1	5,02
C ₆ H ₅ [8] 4-CH ₃ OC ₆ H ₄	93 92,8	68-69 (18) 95-96 (3)	1740	-11,7 -12,5	-61,5 -50,9	43,42	2,71	1	5,39	C ₁₁ H ₈ F ₇ NO	43,56	2,97	1	4,62
4-N02C6H4	** 02	112114 (3)	1740 1740	-13,0	55,4	37,99	1,67	42,66	9,02	$C_{10}H_5F_7N_2O_2$	37,73	1,57	41,82	8,80
2,4,6-(CH ₃) ₃ C ₆ H ₂	84	72-74 (3)	1100	7 67	A F	76 07	04 6	07 67	06 7	N A F	40 K9	08 6	66 67	77 7
N(CH ₃)2 NHC ₆ H ₅	57 85	59-60 (70) 81-82 (6)	1680	-11,4 -11,4 -12,8		40,04 29,9 41,75	2,23	55,62	12,0	$C_{0}^{13}H_{7}F_{7}N_{2}$ $C_{0}H_{7}F_{7}N_{2}$ $C_{10}H_{7}F_{7}N_{2}$	30,0 30,0 41,67	2,43	55,41	11,67 9,72
			0201	21182										
				•			•							

TABLE 1. $(CF_3)_2 CHCF = NR$ (II)

* Triplet, JCF₃-H ≈JCF-H≈8 Hz,
 † Undeciphered multiplet.
 ‡ The reaction was run in dibutyl ether.
 ** The reaction was run in acctonitrile.

TABLE 2. $(CF_3)_2 C = C = NR$ (III)

والمراجعة المتعادية والمتعادية والمحادث المتحاد والمحادث والمحادث والمحادث والمحادث والمحادث والمحادث				IR spec-	19E NIMP			1						
æ	Yield,	Bp,°C	n (I) (n	trum	spectrum		Foun	o%,bi		Empirical		Calcula	ted, %	
4	%	(p, mm Hg)	- (x) (T-	$v_{\rm C=C=N}^{\nu_{\rm cm}^{-1}}$	(in CC14)	υ	н	ų	z	formula	c	н	 F4	z
C ₈ H ₆	28	110-112	1.3409 (25)	2440	7 22-	35 67	2.55	1	6 79	C.H.F.N	35.2	2, 43		6.82
C4H, [6]	20	71-73(60)	1,3632 (25)	2120	-21.4	2		47.98	-	C.H.F.N	1	1	48.43	-
$C_{6H_{11}}$	49	80-81(15)	1,3977 (22)	2098	-23.1	46,33	4,16	44.0	5,43	C, H, F, N	46,33	4.24	44,01	5,41
C ₆ H ₅ [4]	06	70 - 71(14)	1,4462 (22)	2080	-22,0									
4-CH ₃ OC ₆ H ₄	87,5	9496(3)	1	2130	-21,7	46,61	2,35	40,32		C ₁₁ H ₇ F ₆ NO	46,64	2,47	40,28	1
2,4,0-(UI3)3U6H2	7/	82-83(3)												
+		mp 35-37		2120	-23,0	52,92	3,72		5,08	C ₁₃ H ₁₁ F ₆ N	52,88	3,72	1	4,74
N(CH ₃) ₂ 1	45	63-64(87)	1	2000	-19,8	32,73	2,73	51,8	1	C ₆ H ₆ F ₆ N ₂	32,76	3,12	50,66	١

• Singlet. \dagger Based on the data of the IR spectra, the compound dimerizes almost completely when stored for 3 days at 20°.

b) To 3.4 g of the N-phenylimidoyl fluoride (II), 4 ml of pyridine was added. After 4 months the precipitate was filtered to give 0.2 g (6.4%) of the symmetrical dimer with mp 210-212°, which was identical with an authentic specimen [3]. Based on the ¹⁹F NMR and GLC data, the filtrate represents a pyridine solution of the phenylimidoyl fluoride (II), contaminated with a small amount of N-phenylbis(trifluoro-methyl)ketenimine.

CONCLUSIONS

1. Methods were developed for the synthesis of bis(trifluoromethyl)ketenimines by the reaction of perfluoroisobutylene with primary amines, or by the dehydrofluorination of the imidoyl fluorides of α -hydroperfluoroisobutyric acid.

2. The perfluoroisobutylene-triethylamine mixture is a mild dehydrofluorinating agent.

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